COSMETICS AND THEIR RELATION TO DRUGS

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INTRODUCTION

Under the Food, Drug, and Cosmetics Act (FDCA, 21 U.S. Code 301), the Food and Drug Administration (FDC) of the United States has the authority to regulate foods, prescription (Rx) drugs, over-the-counter (OTC) drugs, and cosmetics. The FDA also administers a second statute, the Fair Packaging and Labeling Act (FPLA, 15 U.S. Code 1400). In order to administer this complex task, the FDA depends on the legalistic and statutory definitions of drug and cosmetics in the FDCA. Nevertheless, the public's interpretation of what constitutes a drug or a cosmetic may differ somewhat from that of regulatory agencies. Philosophically and historically, a cosmetic is a product that helps improve external appearance and has the ability to hide, or at least distract from, unwanted stigmata or skin defects.

A product that changes the color of hair is a cosmetic, as is a product intended to increase the skin's tendency to tan by exposure to sun. This traditional view remains ingrained in the consumer's mind but may not be judicially valid. A change in hair color, for example, can be effected by the following: 1) a wig, which might be viewed as an article of clothing; 2) a variety of dyeing processes, which are properly identified as cosmetic changes; and 3) possibly by a variety of ingested or topically applied substances that gradually alter the hair follicle's ability to synthesize melanin, which should be classified as a drug effect. The common goal of these three approaches is to effect a change in appearance, the key objective of all cosmetics. The method by which this goal is achieved differentiates the three hair "coloring" processes and makes a product a drug or a cosmetic. This can create some confusion, as is demonstrated by a consideration of sunscreen products. Sunburn prevention by topical products was for years considered within the scope of cosmetics, even though ultraviolet-B (UV-B) light absorbers were incorporated into these "cosmetics." The cosmetic industry responded rather calmly when the FDA's review of OTC drugs included suntan preparations and sunburn preventives. What for years had been a cosmetic suddenly became a drug by legislative or administrative fiat. The FDA's rationale is justifiably based on the concept that sunburn prevention is prevention of disease. Adding an ingredient that enhances the ability of melanocytes to produce melanin in the skin would be viewed as a cosmetic by the user. The FDA is likely to accept cosmetic (color change, appearance) claims for such a product, but a definition of a drug would become mandatory if the melanin is claimed to protect against sunburn. The implication that a parasol intended to prevent exposure to sun is a medical device has not been judicially examined.

One must recognize that the differentiation between cosmetics and drugs is complex and is blurred by the interplay of consumer perception, commercial interest, and statutory interpretation by regulatory agencies, with the ultimate decision in the hands of the judiciary. For these reasons, differences between drugs and cosmetics are discussed in the next section on the basis of existing U.S. laws, the product's composition, and safety and efficacy. Laws and rules covering the distinction between cosmetics and drugs differ from country to country. For this reason, marked divergence from U.S. practices will be noted in this survey.

COMPARISON ON THE BASIS OF U.S. LAW

Definitions

The sharpest distinction between a drug and a cosmetic is based on the statutory definitions in the Federal Food Drug and Cosmetic Act (21 USC 301 et seq.). Cosmetics are clearly defined as:

> 1) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and 2) articles intended for use as a component of any such articles; except that such term shall not include soap.

On the other hand, drugs are defined as follows:

> The term drug means: (A) articles recognized in the official United States Pharmacopoeia, official

> Homeopathic Pharmacopoeia of the United States or official National Formulary or any supplement to any of them; and (B) articles intended for the use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animal; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any articles specified in clause (A), (B), or (C); but does not include devices or their components, parts, or accessories.

These definitions may differ from the interpretation of the consumer or from generally accepted usage, but courts will adjudicate exclusively on the basis of these statutory definitions. It is clearly the intent of the product, not necessarily its performance, that is used judicially to classify a product as a drug or as a cosmetic. A skin-care product intended to beautify by the removal of wrinkles is both a cosmetic (alters the appearance) and a drug (affects a body structure). Historically and intuitively, the requirements for a drug are more stringent than those for a cosmetic, and the regulatory agency and the courts tend to apply the more stringent requirement to a product that may be perceived to be both a drug and a cosmetic. Table 1 includes a listing of products classified by the FDA as cosmetics. Some of the products are considered drugs or quasi-drugs in other countries.

The Food and Drug Administration's Tasks

The FDA is authorized to enforce the FDCA and the FPLA. The FDA's tools include inspection and seizure, which may be applied equally to drugs or cosmetics. The FDCA prohibits the use (or presence) of poisonous or deleterious substances. Their presence makes a cosmetic "adulterated" or "misbranded." In this regard, no significant distinction is made between drugs and cosmetics. Similarly, good manufacturing practices (GMPs) are applicable to drugs and with minor changes to cosmetics. Products that are manufactured under conditions that are in violation of the GMPs may become subject to seizure. In recent years, the FDA has not initiated formal cases against violators of cosmetic regulations; instead, the FDA has relied on so-called Warning Letters to obtain compliance without recourse to complicated legal action.

In contrast to Rx drugs, OTC drugs and cosmetics are not subject to preclearance. Preclearance is specifically designed to prevent the introduction of dangerous or undesirable drug entities into the market. The restrictions on ingredients are most severe in the case of OTC drugs and preclude introduction of untested drugs or combinations. In fact, a "new chemical entity," which might be entirely suitable for introduction as an OTC drug, requires workup via the new drug application (NDA) process. The approval of Rx and OTC drugs by the FDA is, in principle, based on the performance of the drug entity. Efficacy against the disease, bioavailability, and lack of adverse side effects are of primary importance. Thus, judicious choice of drug excipients is required for all drug approvals. Nevertheless, in the absence of an FDA-approved list of cosmetic ingredients, the cosmetic manufacturer has the responsibility to provide products that are not injurious to the user under the expected conditions of use. Some ingredients are specifically restricted, and a regulation requiring safety substantiation exists. These will be discussed in the section entitled "Restrictions on the Use of Ingredients."

Table 1 List of products (recognized as cosmetics in the United States)

Baby preparations	Creams, lotions, oil, powders, shampoos
Bath preparations	Bubble baths, capsules, oils, salts, soaps and detergents, tablets
Cleansing preparations	Creams, douches, liquids and pads, lotions, personal cleansing products
Dentifrices	Aerosols, breath fresheners, liquids, mouthwashes, pastes, powders
Fragrance products	Colognes and toilet waters, deodorants, fragrances, perfumes
Hair products	Depilatories, dressings, dyes and colors, grooming aids, lighteners, miscellaneous rinses, permanent wave products, shampoos, sprays, straighteners, tints, tonics, wave sets
Makeup preparations	Blushers, eyebrow pencils, eyeliners, eye makeup preparations, eye makeup removers, eye shadows, face powders, facial makeups, fixatives, foundation makeups, leg and body paints, lip glosses, lipsticks, mascaras, rouges
Miscellaneous products	Paste masks, powders (men's, women's, talcums)
Shaving preparations	Aftershaves, beard softeners, shaving creams (aerosol, brushless lather), preshaves
Skin care preparations	Body and hand preparations (moisturizers), eye creams, face and neck preparations, fresheners and astringents, suntan gels

Color Additives

Color additives are of particular importance to the formulation of cosmetics. Dyes and pigments not only make products more attractive but also are vital to any product that is intended to alter the color of any part of the body. Color additives are regulated meticulously by the FDA, and only some general information on the current regulatory status of colorants in the United States can be provided.

Certified color additives are synthetic organic dyes that are described in an approved color additive petition. Each manufactured lot of a certified dye must be analyzed and certified by the FDA prior to usage.

Color lakes are pigments that generally consist of an insoluble metallic salt of a certified color additive deposited on an inert substrate. These lakes are subject to the color additive regulations of the FDA and must be certified by the agency prior to use.

Color additives that are not classified as certified color or color lakes are identified as *noncertified color additives*. Each of these substances is the subject of an approved color additive petition, but individual batches do not require certification by FDA prior to use.

The fourth major class of color additives is *hair colorants*. These compounds or their mixtures may be used only to color scalp hair and may not be used in the eye area. Use of these colorants is "exempt," that is, the so-called coal-tar hair dyes may be sold with cautionary labeling, directions for preliminary (patch) testing, and restrictions against use in or near the eye.

Soap Exclusion

Soap is specifically excluded from cosmetics in the FDCA, and no cosmetic or drug regulations are applicable to soap. The FDCA fails to define the term *soap*, but the FDA has ruled that a product is a soap if the bulk of the nonvolatile matter is the alkali salt of a fatty acid and if its detersive properties are due exclusively to the fatty acid salt. In addition, the product must be labeled as a soap. A product is identified as a shampoo when it consists, e.g., only of aqueous potassium oleate. It then must conform to cosmetic regulations.

The term *soap* thus has two meanings. The first is the FDA's definition, which is used for legal purposes. The second is the generic sense, whereby soaps may refer to cleansing products that may not meet the specifics of FDA's definition. Such products must, therefore, be labeled as cosmetics. The Federal Trade Commission (FTC) and the Consumer Products Safety Commission (CPSC) handle the regulatory control for soaps.

COMPARISON ON THE BASIS OF COMPOSITION

Drug Ingredients Versus Cosmetic Ingredients

On the basis of the Drug Efficacy Study Implementation (DESI) review, which began in 1962, the FDA ultimately concluded that of about 16,000 claims made for 3400 Rx drugs, only about 2300 drugs were effective for at least one indication. Today, Rx drugs must undergo the NDA process, which, for all practical purposes, is a critical preclearance procedure. As the work on the DESI review neared completion, the FDA initiated the so-called OTC review in 1972. The FDA classified some 250,000 drugs into about 55 therapeutic groups. The panels that reviewed each group had the responsibility to establish the safety and efficacy of each OTC drug and to restrict claims for these drugs to those the panel considered appropriate for a given drug or combination of drugs. It is apparent that the marketability of a drug—Rx or OTC—requires the presence and bioavailability of an identifiable drug entity that can be expected to exert some therapeutic benefit. No such legal requirement for the use of raw materials exists in cosmetics. As a rule, the presence of and claim for any component in a cosmetic that may have a therapeutic effect converts such a cosmetic into a drug.

The FDA has classified the following topically applied products as OTC drugs on the basis of safety and efficacy review of the drug(s) constituents:

- Acne products
- Antidandruff products
- Antimicrobial products
- Antiperspirant products
- Astringent products
- Oral care products
- Skin-protectant products
- Sunscreen products
- External analgesic products

In other countries, some of these products are considered cosmetics.

Some of the actives used in the past in such products have been classified as Category I, i.e., safe and effective. Usage of these agents and the claims made for the finished product make these products OTC drugs, not cosmetics.

The activities of the OTC panels are not yet completed, although most of the tentative final reports have been published. However, no definitive rulings have been made or subjected to judicial review. It appears at this time that the ingredients reviewed by the OTC panels can be used in cosmetics as excipients and the like. To repeat, their use, together with drug or therapeutic claims, transforms the cosmetic into a drug, in which case the labeling and claim

structure must conform to those established for OTC drugs. The designation "cosmetic" places almost no restriction on the use of components. However, claims for therapeutic efficacy convert any cosmetic into a drug, as interpreted by the FDA. The regulations do not restrict the use of a drug substance for purposes unrelated to its drug status.

COSMETICS AND THEIR RELATION TO DRUGS

Restrictions on the Use of Ingredients in Cosmetics

The review of active drugs by the OTC panels was limited to relatively few drug entities, but the cosmetic industry employs thousands of ingredients, including many of plant and animal origin. Many typical cosmetic ingredients are identical to the components used in Rx and OTC drugs, but only very few cosmetic ingredients are subject to restrictions by the FDA. These include mercury compounds, except those used as preservatives in products intended for use in or near the eye. Others are bithionol, vinyl chloride, halogenated salicylanilides, zirconium compounds in aerosol products, chloroform, chlorofluorcarbon propellants, and hexachlorophene. With regard to cosmetic ingredients, the FDA has placed the responsibility for substantiating their safety squarely on the producer. Such safety substantiation also includes finished products. Each ingredient used in a cosmetic product and each finished cosmetic product shall be adequately substantiated for safety prior to marketing. Any such ingredient or product whose safety is not adequately substantiated prior to marketing is misbranded unless it contains the following conspicuous statement on the principal display panel: Warning—The safety of this product has not been substantiated [21 CFR, Par. 740].

These regulatory activities and the need to demonstrate to the public that the cosmetic industry as a whole is prepared to accept responsibility prompted the Cosmetics, Toiletries and Fragrance Association (CTFA) in 1976 to establish the Cosmetic Ingredient Review (CIR) for the purpose of evaluation and review of the safety of the ingredients used in cosmetics. The CIR process established a system for prioritizing ingredients based on frequency of use, concentration used, area of use, frequency of application, use by sensitive subgroups, likelihood of biologic activity, and consumer complaints. This is a scientific review of worldwide data, and nonvoting members from industry and consumer groups participate in the deliberations. In order to speed up the review process and to avoid duplication, the CIR expert panel may defer study of substances that are already under review by other safety programs. The most important of these are those by the Research Institute for Fragrance Materials (RIFM) and the Flavor and Extract Manufacturers Association (FEMA). The former establishes the safety of fragrance components; its funding and concept permit expenditures for safety testing of substances. The latter addresses issues related to the safety of individual flavor materials. The reviews by the CIR panel are available from the CTFA (1101 17th St., N. W., Washington, D.C., 20036-4702) and have appeared over a period of years in the *Journal of the American College of Toxicology*.

Although the CIR process is sponsored by the CTFA, the latter will conduct safety studies for substances considered crucial to the survival of the cosmetic industry. The CTFA will also establish and pay for research required to confirm the stability, chemical purity, and safety of various cosmetic ingredients. These activities are part of the cosmetic industry's technically oriented self-regulation program. Similar programs exist in the pharmaceutical industry.

RIFM has recommended discontinuance of the use of acetylethyl tetramethyltetralin, 6-methylcoumarin, musk ambrette, and musk ketone. Another self-imposed ingredient restriction concerns the use of potential nitrosating agents in products containing various (secondary) alkanol amines, in light of the hazard of nitrosamine formation. In the European Union, (E.U.), the use of *tri-* and *di*-ethanolamine is restricted.

One of the key self-regulatory procedures in the cosmetic industry is the voluntary reporting process of adverse reactions. The program is intended to provide data on the type and frequency of adverse reactions reported by consumers or by their medical advisors to the industry. It is an important means of detecting problems that are not treated in hospital emergency rooms (i.e., documented in the National Electronic Injury Surveillance System, NEISS) or do not reach poison control centers.

Practical Aspects

For practicing formulators, the border between cosmetics and drugs is not clear. Drug entities for which claims are made on the label differentiate drugs from cosmetics. However, the same or chemically similar excipients and formulation aids are widely used in cosmetics and drugs. Finally, one must recognize that cosmetics may include groups of substances not normally found in drugs. These similarities and differences are illustrated in Table 2. Substances considered drugs by U.S. law have been excluded from the table. This listing is not comprehensive and is presented for illustrative purposes only.

Table 2 Common usage of selected ingredients in cosmetics and drugs and cosmetics

Function	Cosmetics (primarily)	Cosmetics and Drugs
Abrasive	Oatmeal	Dicalcium phosphate
Absorbent		Kaolin, silica
Antifoam		Simethicone
Antioxidant		Ascorbic acid, BHA, BHT, tocopherol
Antistatic	N-Lauroyl-β-Alanine, stearyldimethylbenzylammonium chloride [INCI nomenclature: CAS 68650-39-5]	
Binder		Hydrophilic gums, Polyvinyl acetate, starch
Bulking agent		Cellulose, silica
Chelator		Citrates, EDTA and salts, glucuronic acid
Cleanser	Triethanolamine laurylethersulfate, lauryl betaine	Sodium Laurylsulfate, poloxamer 188
Coemulsifier	Beeswax	Fatty alcohols
Emollient	Apricot kernel oil	Cocoa butter, dibutyl sebacate, dioctyl adipate, isopropyl myristate, lanolin, mineral oil, squalene
Emusifier	Sodium lauroyllactylate [INCI nomenclature: CAS 13557-75-0]	Alkoxylated fatty acids, alkoxylated fatty alcohols, fatty acid salt, lecithin, monoglycerides, poloxamers, polysorbates, sorbitan esters
Folkoric additive	Plant and animal extracts, protein derivatives	
Humectant	N-Acetoyl monoethanol-amide, pyrrolidone carboxylic-acid	Glycerin, sorbitol, urea, sodium lactate
Lubricant (hair and skin)	Mink oil, sodium hyaluronate	Coconut oil, lanolin, olive oil, petrolatum
Plasticizer	Ethyltoluenesulfonamide	Camphor, dioctyl sebacate
Preservative	1,3-Dimethylol-5, 5-dimethyl hydantoin, Quaternium-15 [INCI nomenclature: CAS 4080-31-3]	Imidazolidinyl urea, parabens phenoxyethanol
Solvent and viscosity reducer		Acetone, ethanol, ethyl acetate, glycerin, hexylene glycol, *i*-Propanol, propylene glycol, toluene
Suspending agent	Sodium methylnaphthalene sulfonate [INCI nomenclature: CAS 26264-58-4]	Carbomer, cellulose drivatives, clays
Thickener		Behenyl alcohol, polyethylene, polyisobutene, polyoxyethylene 14,000, tristearin
UV light absorber	Butyl methoxybenzoylmethane	Drometrizole

The overlap on the basis of ingredient usage is apparent from an examination of column 3.

Labeling of Cosmetics

An important ingredient-related topic is cosmetic ingredient labeling. Advocates of consumers' rights have suggested that the public would benefit from full disclosure of the composition of cosmetic products. Pursuant to the regulations by the FDA and the FPLA, all cosmetics are now required to carry the following information on labels: 1) a statement of the identity of the product; 2) a statement of the net quantity of contents; 3) a statement of the name and place of business of the manufacturer, packer, or distributor; 4) a list of the ingredients included in the product in order of predominance; and 5) cautionary or warning language [21 USC 321 (k); 15 USC 1459 (b); 21 CFR 701.10].

Except the aforementioned labeling for item 4, similar requirements exist for Rx and OTC products at the time of this writing. Labeling of all constituents in OTC drug products is still under consideration. The listing of ingredients in cosmetics must be in descending order of predominance, with some exceptions for components present as minor constituent and color additives. In order to achieve uniformity for identification, the CTFA has continuously created shorthand nomenclature for all cosmetic ingredients. The "naming" process is similar to that employed by USAN (U.S. Adopted Name). Many names and chemical descriptions of cosmetic ingredients have been reviewed and accepted by the FDA (for the purpose of using these names on labels). As a result, cosmetics in the U.S. are now labeled in accordance with the nomenclature and the rules of the International Nomenclature of Cosmetic Ingredient Dictionary (INCI Dictionary; 1). This approach has been accepted in the E.U., where the same names (with minor modifications) are used. "Harmonization" of names is a continuing process to make these names linguistically acceptable throughout the world.

COMPARISON ON THE BASIS OF SAFETY AND PERFORMANCE

Safety

Users know that, as a rule, Rx drugs are more likely to cause adverse side effects than OTC drugs. This is an obvious result of the nature and of the distribution system for these products. Prescription drugs are administered under the supervision of a physician, who has the responsibility and moral obligation to monitor the patient's progress. However, OTC drugs may be used ad lib by the uninformed, who may not always be competent to diagnose the underlying disease or to recognize adverse side effects. In this respect, cosmetics resemble OTC drugs except that cosmetics are used repeatedly and over extended periods of time. Thus, the requirements for the safety of cosmetics should be, in fact, much more stringent then those for many drugs. The level of side effects or adverse effects that can be tolerated by manufacturers of cosmetics is virtually nil. Of particular concern is the sensitizing potential of components during prolonged and repeated use. Photosensitization is another phenomenon that has led to the removal of some cosmetic ingredients from the list of routinely employed substances.

Elegance

Elegance is not a primary concern in the case of Rx drugs but impacts marketing of OTC drugs and helps to ensure patient compliance. By contrast, any feature that detracts from the elegance (appearance, odor, texture, etc.) of a cosmetic interferes with its marketability and acceptance. As a matter of fact, cosmetic elegance is the essential attribute of a successful cosmetic product.

Performance

Performance is the one issue in which cosmetics and drugs are different. Drug efficacy is assessed on the basis of cure or prevention of disease. The FDA has established that cosmetic products that exert therapeutic effects are drugs. As a result, some traditional cosmetics were converted into drugs via the OTC panel process. Any performance claims for these OTC products are limited to the wording approved during the OTC review process.

Claims for (nondrug) cosmetics may be, for example, fashion-oriented (color), beauty-oriented (hiding of blemishes), or texture-oriented (emollient or lubricant). These, and related claims, are easily perceived and can be readily documented. More complex issues arise when cosmetic claims are made for age-related or reparative skin-care preparations. In the past, various regulatory agencies have been permissive with regard to cosmetic puffery claims. More recently, claims made for some cosmetics suggest to consumers that the product may exhibit a druglike effect, as defined by statute. A Commissioner of Food and Drugs has labeled these claims "daring" (2). Advertising copy that implies that a product nourishes the skin, is active, causes tingling, tightens the skin, discourages wrinkle formation, is prepared by a pharmaceutical company, or performs like

a face-lift may be false and misleading if the product does not perform. On the other hand, the product is considered a drug if it performs as claimed. Aside from drug results, claims for skin or hair benefits require documentation for commercial purposes (advertising and promotion). Thus, claims for performance are likely to run afoul of FTC rules. In the E.U., however, claims for efficacy require substantitation by regulation. Guidelines for documenting cosmetic performance exist in Europe but not in the United States (3). On the other hand, the FDA has a powerful tool for stopping unsubstantiated claims. A claim for wrinkle "removal," even on a temporary basis, may make a cosmetic product into a drug. Thus, the cosmetic industry is as tightly controlled as the Rx industry. Whenever a new indication for an existing drug constituent is claimed or whenever a druglike claim is made for *any* ingredient, a new drug application is required.

Shelf Life

Cosmetic preparations need not be labeled for outdating. This does not imply that cosmetic products must (or do) exhibit indefinite stability. The physical and chemical stability of cosmetics is routinely studied by the same procedures as those used for Rx or OTC drugs. Since cosmetic products do not contain active drug entities, the chemical stability of *any* component may be critical to the performance of the product: The components of a fragrance product require monitoring; the performance of a hair-waving preparation may depend on alkalinity and the chemical integrity of the reducing agent.

Physical stability affects cosmetic elegance, for example, by the breaking of an emulsion. Moreover, physical stability may also affect efficacy, as is the case during settling of a pigment in a nail lacquer that might then no longer be readily redispersible. A similar type of instability may occur as a result of the settling of an antiperspirant compound in a suspension aerosol. In these cases, neither the cosmetic (nail lacquer) or the OTC drug (antiperspirant) performs as claimed and may be considered misbranded or mislabeled.

As a rule, therefore, the demands of chemical and physical stability are similar for drugs and cosmetics. Under certain circumstances, the demands on physical stability may be especially critical as, for example, in hand and body lotions that have to perform under tropical conditions after having been exposed to the heat of the sun on the beach or after storage under arctic conditions in a ski hut.

The criteria for microbiologic cleanliness of cosmetic products are especially complex. Like a drug, a cosmetic is deemed adulterated if: 1) it bears or contains any poisonous or deleterious substance which may render it injurious to users on the conditions of use as are customary or usual; 2) it contains in whole or in part of any filthy, putrid, or decomposed substance; and 3) if it has been prepared, packed, or held under unsanitary conditions where it may have become contaminated with filth, or whereby it may have been rendered injurious to health [Sect. 601, FDCA].

Cosmetic companies adhere to FDA-mandated GMPs or to GMPs promulgated by the CTFA with regard to housekeeping, cleaning, and sanitizing of equipment, and purity of raw materials and process water. Water is a particularly important component of finished cosmetics. Its purity is closely monitored to avoid the inadvertent introduction of contaminating biota into products. The GMPs established by the FDA are available in 21 CFR, Part 211, and the CTFA has published similar recommendations in the form of Quality Assurance Guidelines for Cosmetic Manufacture.

The final check on purity is on the finished product. The high water content and the inclusion of nutrients for unwanted microbiota make cosmetics subject to microbiological contamination. Thus, topical OTC products and cosmetics require preservation and a final check before distribution. Preservative systems and GMPs usually ensure delivery of essentially uncontaminated cosmetics. The microbiologic requirements recommended by the CTFA include the following: 1) baby products: less than 500 microorganisms/g; 2) eye products: less than 500 microorganisms/g; 3) oral products: less than 1000 microorganisms/g; (4) all other products: less than 1000 microorganisms/g; and 5) pathogens should be absent.

The use of preservatives to achieve the desired low levels of contaminating microorganisms is required. Some liquid cosmetic products do not support the growth of microorganisms (e.g., alcohol-based aftershave), while others are excellent growth substrates (e.g., a protein-containing hair conditioner). Because consumers frequently introduce microorganisms during normal product use, some cosmetic manufacturers may require that their products be self-sterilizing. This is a difficult task and not always achievable. A final check for levels of microorganisms is, nevertheless, desirable.

Relation to Health-Care Providers

Like the drug industry, the cosmetic industry requires animal toxicology and human testing to establish the safety of its products. As a rule, most cosmetic products are quite innocuous upon ingestion, even though they may cause laxation or act as emetics. The industry makes a deliberative effort not to market products that might elicit

toxic syndromes when ingested or applied topically. The former type of problem is usually handled by poison control centers and routinely (in 90% of all cases) involves ingestion by children. The number of fatalities was reported as nil between 1971 and 1978.

Dermatologists see many patients who have used cosmetic products properly but still report adverse reactions. The cosmetic industry is conscious of the need to provide products that do not elicit irritation or allergic responses during use. For this reason, the cosmetic industry depends on all types of patch and related testing by dermatologic laboratories to establish the safety of a given product in a predictive fashion. A whole battery of test protocols is available, and hundreds of subjects are tested routinely by dermatologists before product marketing (4).

Topical drugs and cosmetics have the potential of penetrating the skin. In the case of a topical drug (e.g., an antiinflammatory steroid), localized permeation may be a desirable feature. Penetration of cosmetics into and through the skin may elicit undesirable effects, especially since consumers may apply two or more products to the same site. Thus, in contrast to topically used Rx drugs, cosmetics should be retained on the skin with minimal penetration. Dermatologists also recommend cosmetics to patients as, for example, in cases of dry or chapped skin. Clearly, the cosmetic industry–physician–user relationship is not very different from that existing in the drug industry.

COSMETIC OR DRUG?

Formulators and marketers require an answer to the question of whether a given product is a cosmetic or a drug. Some of the answers are almost obvious. In the United States, a product is a drug if a drug claim is made for the preparation. The inclusion of a new chemical entity on which a therapeutic claim is based requires filing of a NDA; a product containing such a substance is automatically viewed as a drug. A typical example is a suntan product that adds an UV light-absorbing substance that was not reviewed by the OTC panel but was previously used as a sunscreen. Although the product in question was labeled as a drug, the FDA ruled that this clearly constituted use of an unapproved *new* drug substance. The addition of an OTC-reviewed sunscreen into a cosmetic makeup preparation—without claims for sun-protective action but with the indication that the product contains a sunscreen for the purpose of reducing UV light-induced skin aging—could be considered a drug use in the United States.

A soap to which an OTC Category I antimicrobial agent has been added is converted into a drug. This raises an interesting secondary issue. Soaps may be tinted with noncertified color additives. This inclusion of the antimicrobial requires not only drug labeling but also reformulation with approved colorants.

As a rule, the status of the product is determined by the claims made for it and its intended purpose. The use of aluminum chloride, a Category I OTC antiperspirant, as an astringent probably does not confer drug status on the product. It was already noted that certain OTC Category I skin protectants, such as petrolatum, can be used freely in cosmetics as long as no drug claims are made for the product. Numerous other issues might arise, and each one might require specific adjudication. An example is the use of an approved sunscreen in a cosmetic product to preserve it against UV light deterioration. Since the intent of the sunscreen's use is clearly not drug related, the product will probably be considered a cosmetic.

SUMMARY

Cosmetics and drugs are distinctly different on the basis of U.S. law. In principle, cosmetics may not contain ingredients that treat or prevent disease or alter the structure or function of the human body. The objective of cosmetics is limited to the enhancement of appearance.

The ingredients used in cosmetics to a large extent are the same as those employed in drugs, with the exception of components that are intended to cure, alleviate, or prevent disease.

The demands on product stability and manufacturing practices are essentially the same for cosmetics and drugs.

Finally, important differences are seen in judging the performance of cosmetics and of drugs. Consumers assess cosmetics based on the products' performance vis-à-vis the demand for better appearance. On the other hand, drugs are assessed on their ability to prevent or improve a disease state.

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